UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|---|---|---|---|---|
| 10/596,734 | 04/03/2007 | Larry E. Arthaud | ILEX:096US/10606835 | 9958 |

32425 7590 10/06/2009

FULBRIGHT & JAWORSKI L.L.P.
600 CONGRESS AVE.
SUITE 2400
AUSTIN, TX 78701

| EXAMINER | |
|---|---|
| DIBRINO, MARIANNE NMN | |

| ART UNIT | PAPER NUMBER |
|---|---|
| 1644 | |

| MAIL DATE | DELIVERY MODE |
|---|---|
| 10/06/2009 | PAPER |

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 10/596,734 | ARTHAUD, LARRY E. | |
| | Examiner | Art Unit | |
| | MARIANNE DIBRINO | 1644 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *22 June 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *1-4* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-4* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☒ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *10/23/06, 10/04/07*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

**DETAILED ACTION**

1. Applicant's amendment filed 6/22/06 is acknowledged and has been entered.

2. The listing of references in the specification is not a proper information disclosure statement. 37 CFR 1.98(b) requires a list of all patents, publications, or other information submitted for consideration by the Office, and MPEP § 609.04(a) states, "the list may not be incorporated into the specification but must be submitted in a separate paper." Therefore, unless the references have been cited by the examiner on form PTO-892, they have not been considered.

3. The oath or declaration is defective. A new oath or declaration in compliance with 37 CFR 1.67(a) identifying this application by application number and filing date is required. See MPEP §§ 602.01 and 602.02. The oath or declaration is defective because: Non-initialed and/or non-dated alterations have been made to the oath or declaration. Specifically, the changes to the inventor's Country of Citizenship and Residence Address have not been dated. See 37 CFR 1.52(c).

4. It is noted by the Examiner that Applicant's ADA filed 6/22/06 has the wrong date listed for the filing date of the provisional 60/532,059 application, *i.e.,* "2006-06-22" should be 2003-12-22".

5. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. Claims 1-4 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The specification does not disclose how to make and/or use the instant invention, a method for the prevention or treatment of Type 1 diabetes mellitus in a prediabetic human subject, said method comprising administering to said subject an effective amount of an anti-CD52 antibody, including wherein said anti-CD52 antibody is CAMPATH-1H. The specification has not enabled the breadth of the claimed invention because the claims encompass preventing or treating type 1 diabetes mellitus. The state of the art is such that it is unpredictable in the absence of appropriate evidence whether the claimed method can be used for prophylaxis or for treatment. The specification discloses no working examples with regards to the use of the instant invention for prevention or treatment of said disease *in vivo*.

To be enabling, the specification of a patent must teach those skilled in the art how to make and use the full scope of the claimed invention without 'undue experimentation.'" Genentech, Inc. v. Novo Nordisk, A/S, 108F.3d 1361, 1365, 42 USPQ2d 1001, 1004 (Fed. Cir. 1997) (quoting In re Wright, 999F2d 1557, 1561, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993)). In In re Wands 8 USPQ2d 1400 (CAFC 1988), a number of factors are set forth which a court may consider in determining whether a disclosure would require undue experimentation. These factors were set forth as follows: (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims. All the factors need not be reviewed when determining whether a disclosure is enabling. Amgen, Inc. v. Chugai Pharm. Co., Ltd., 927F2.d 1200, 1213, 18 USPQ2d 1016, 1027 (Fed. Cir. 1991) (noting that the Wands factors "are illustrative, not mandatory. What is relevant depends upon the facts.").

The specification discloses that Type 1 diabetes mellitus, IDDM, is a chronic, organ-specific autoimmune disease resulting from the selective destruction of the insulin-producing β islet cells of the pancreas. The specification discloses in humans, progression from diagnosis of disease to complete β islet destruction takes several years. The specification discloses that autoantibodies to β islet antigens such as GAD65 and IA-2 and insulin are produced and can be detected in the blood several years prior to onset of IDDM (second paragraph on page 1). The specification further discloses that the etiology of IDDM is unkown, but based upon analysis in the NOD mouse and BB rat, the disease is believed to be mediated by TH1 subset of T lymphocytes and that dendritic cells, macrophages, NK cells and B cells accumulate at the site of cell destruction and may play a role in the development of the disease, while in animal models, pro-inflammatory cytokines such as IFN-γ TNF-α and IL-1 have been shown to exacerbate the disease effects (third paragraph on page 1).

The specification discloses that CAMPATH-1H, also known as Alemtuzumab and MABCAMPATH, and approved for the treatment of B-cell chronic lymphocytic leukemia, induces the rapid fall of lymphocyte and monocytes counts over the first hour post-infusion resulting in a prolonged lymphopenia that ensues for over 2 years (last sentence on page 2).

The specification discloses in a prophetic manner, administering anti-CD52 antibodies, preferably CAMPATH-1H, to a patient with type 1 diabetes in the range of about 10 to about 150 mg over a period from 1 to about 20 days (paragraph spanning pages 3-4). The specification further discloses that a course of CAMPATH-1H treatment has been associated with a reversible exacerbation of existing neurological symptoms and activation of asymptomatic lesions caused by antibody-induced release of cytokines [in multiple sclerosis].

The specification also discloses recruiting first-degree relatives of individuals diagnosed with IDDM for trials directed at prevention of progress in prediabetic individuals, as well as testing for levels of islet cell antibody, GAD and IA-2 (Section A on pages 4-5).

Evidentiary reference Colagiuri (Diabetes Voice 12/02 47(4): 18-20) teaches "For Type 1 diabetes, preventative research holds some promise, but much work is needed before preventative treatments can be widely offered to people at risk of Type I diabetes or those with the disease in its early stages." (first paragraph of reference).

Evidentiary reference UPMC (2009) teaches "Currently, there is no known way to prevent type 1 diabetes. Researchers are studying immunosuppressive treatments that may benefit high-risk people." ("Prevention" section on page 4 of 5).

Evidentiary reference Schatz *et al* (Diabetes Care 12/03, 26(12): 3326-3328) teach "Clinical onset of type 1 diabetes is the outcome of a smoldering disease process typically ignited many years earlier, probably soon after birth. Therefore, early disease onset most likely reflects a particularly aggressive and already well-advanced variant of the condition." (page 3326 at column 3, first full paragraph).

Evidentiary reference Merck Manual of Diagnosis and Therapy (17th Ed., Berrs and Berkow, Eds. Merck Res. Lab. Whitehouse Station, N.J. page 165, 1999) teaches that the clinical onset of type I DM may occur years after the insidious onset of the underlying autoimmune process. Merck Manual therefore teaches that the autoimmune process predates the clinical onset, that onset largely representing an endocrine disease rather than an autoimmune disease process.

Thus, the evidentiary references establish unpredictability in the art of preventing and treating type 1 diabetes mellitus, Applicant does not present working examples of preventing said disease using anti-CD52 antibodies, and the claims are broadly drawn to a method for prevention of type 1 diabetes mellitus in a prediabetic human subject.

There is insufficient guidance in the specification as to how to make and/or use instant invention. Undue experimentation would be required of one skilled in the art to practice the instant invention. See In re Wands 8 USPQ2d 1400 (CAFC 1988).

7. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

8. Claim 3 is rejected under 35 U.S.C. 102(b) as being anticipated by WO 92/07084 A1 as evidenced by emedicinehealth.

WO 92/07084 A1 teaches that anti-CDw52 (*i.e.*, anti-CD52) antibody, including CAMPATH-1H, a humanized antibody, is useful for treating juvenile onset diabetes. WO 92/07084 A1 teaches that humanized antibodies more closely resemble human antibodies when administered to a human patient and so do not elicit an anti-antibody response to the same degree, and teaches a method of treating a human having juvenile onset diabetes with the CAMPATH-1H antibody (especially paragraph spanning pages 9-10, page 10 at the first full paragraph, pages 11-12 at the first tow lines, and claims).

Evidentiary reference emedicinehealth teaches "Type 1 diabetes is typically recognized in childhood or adolescence. It used to be known as juvenile-onset diabetes or insulin-dependent diabetes mellitus."

9. Claim 4 is objected to under 37 CFR 1.75 as being a substantial duplicate of claim 2. When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k).

10. No claim is allowed.

11. The reference crossed-out on Applicant's Form 1449 filed 10/23/06 has not been considered by the Examiner as it is not a complete citation, *i.e.*, it is missing a publication date.

12. Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Marianne DiBrino whose telephone number is 571-272-0842. The Examiner can normally be reached on Monday, Tuesday, Thursday and Friday.

If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Ram Shukla, can be reached on 571-272-0735. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Marianne DiBrino, Ph.D.
Patent Examiner
Group 1640/Technology Center 1600
September 29, 2009

/G.R. Ewoldt/
Primary Examiner, Art Unit 1644